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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/244,792	02/05/1999	ALDO T. IACONO	P32130	4164

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EXAMINER	
WANG, SHENGJUN	
ART UNIT	**PAPER NUMBER**
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/244,792	IACONO, ALDO T.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-22,24,30,31 and 49-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-22,24,30,31 and 49-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments, exhibit and remarks submitted June 5, 2007 is acknowledged.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 19-22, 30-31, 49-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waldrep et al. (US 5,958,378) and Fuji et al. (US 6,197,829), in view of Adjei et al. (US 5,635,161), Knight et al. (5,049,388), Gordon et al. (US 6,657,893) and Iacono et al. (Am J, Respir. Crit. Care Med. Vol. 155, pp 1690-1698, 1997, IDS), and in further view of Stanford et al. (EP 0372 541).

3. Waldrep et al. and Fuji et al. teaches that cyclosporine are old and well known in combination with various pharmaceutical carriers and excipients in various dosage forms, particularly, aerosol dosage form. These medicaments are taught as useful as immunosuppressant for treating or preventing graft rejections, inflammation and other immunological mediated conditions such as graft rejections of lung, heart, and other organs, asthma, autoimmune disease, such as rheumatoid arthritis, systemic lupus erythematosis. Specific liposome aerosol dosages are disclosed. The aerosol dosage may be either is solution or in powder forms. See, particularly, the abstract, col. 4, line 22 to col. 5, 64, the examples, col. 13, lines 3-60, and the claims in Waldrep et al. and, column 7, lines 40 to col. 8, lines 59, and the claims in Fuji et al.

Cyclosporine is particularly known to be used with other immunosuppressant for treatment of those disorders. See, the claims in Fuji.

4. Waldrep et al. and Fuji et al. do not teach expressly the various dosage forms, or the dosage levels herein claimed, or the particular time of administration as herein claimed.

However, Adjei et al. teaches that pulmonary delivery of peptide and protein biotherapeutics, such as cyclosporine, by aerosol is well known in the art. Both suspension (solid particle) and solution aerosol formulas are known in the art. propellants are normally used with the aerosol composition. See, particularly, Col. 1, lines 15 to col. 2, line 65, and the examples. Knight et al. teaches that cyclosporine aerosol dosage may be in the form of powder. See, particularly, example 2 therein. Gordon et al. disclosed that dry powder is a well-known form for pulmonary aerosol drug delivery. See, particularly, col. 1, lines 15-67, and the claims. Iacono et al. teaches a cyclosporine composition for aerosol delivery consisting of cyclosporine, a solvent and a propellant and the method of using the same for treating lung graft rejections. See, the whole article, particularly, page 1691, col. 2, the paragraph subtitled "Drug preparation, aerosol generation, and therapy."

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to treating the patients of organ transplantation, either lung, or non-lung transplantation prior to the development of symptoms associated the transplant rejection with the aerosol composition comprising cyclosporine and another immunosuppressant, or treating other patients with inflammatory condition, immunological mediated conditions such as asthma, or rheumatoid arthritis. Stanford et al. teaches that

immunosuppressive agents are known to be useful for reducing the frequency of acute transplant rejections. See, particularly, the abstract, page 3, lines 35-40 and fig. 6.

A person of ordinary skill in the art would have been motivated to treating the patients of organ transplantation, either lung, or non-lung transplantation prior to the development of symptoms associated the transplant rejection with the aerosol composition comprising cyclosporine and another immunosuppressant, or treating other patients with inflammatory condition, immunological mediated conditions such as asthma, or rheumatoid arthritis because cyclosporine are known to be useful for organ transplantation patients and are known for treating inflammatory disease or immunological mediated conditions herein, and are particularly known to be delivered through pulmonary delivery. Further, the cited prior art as a whole teach various aerosol formulation of cyclosporine, encapsulated, or un-encapsulated as an improvement over simple aerosol employment of powdered active ingredient, and the aerosol cyclosporine as useful for an anti-inflammation, anti-rejection medicaments. The skilled artisan would have possessed all conventional administration regimens, and seen the selection of one or another as the simple selection from among obvious alternatives. Further, optimization of a result effective parameter, e.g., effective amount of a therapeutical agent, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215. Further, as disclosed in the prior art, the employment of the particular method disclosed therein is to improve the old and well-known aerosol delivery method. Therefore, employ the compound only without the further employment of carrier as herein recited would have been within the purview of the skilled artisan. As to the recitation of "acute" transplant rejection, note immunosuppressive agents are known to be useful for acute transplant rejections. Further, as to recitation of "chronic refractory" in claim 19, it is

noted that a method known for preventing transplantation rejections would reasonably expected to prevent the development of rejections, either chronic or acute.

5. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Waldrep et al. (US 5,958,378) and Fuji et al. (US 6,197,829), in view of Adjei et al. (US 5,635,161), Knight et al. (5,049,388), Gordon et al. (US 6,657,893) and Iacono et al. (Am J, Respir. Crit. Care Med. Vol. 155, pp 1690-1698, 1997, IDS) for reasons discussed above, and in further view of Armistead et al. (US 5,665,774).

6. Waldrep et al. (US 5,958,378) and Fuji et al. (US 6,197,829), Adjei et al. (US 5,635,161), Knight et al. (5,049,388), Gordon et al. (US 6,657,893) and Iaconó et al. (Am J, Respir. Crit. Care Med. Vol. 155, pp 1690-1698, 1997, IDS) as a whole do not expressly teach the further incorporation of an anti-inflammatory agent for the preventing graft rejections.

7. However, Armistead et al. teaches that steroid is useful in treating or preventing graft rejections. See, particularly the claims.

8. Therefore, it would have been obvious to one of ordinary skill in the art, at the time the claimed invention was made to co-administer the cyclosporine composition with a steroid for preventing graft rejection.

Response to the Arguments

Applicants' amendments and remarks submitted June 5, 2007 have been fully considered, but are not persuasive.

Applicants' argue that the examiner has not established prima facie obviousness. Particularly, applicant contend that the cited references do not provide the disclose of "preventing" the rejections, i.e. administering cyclosporine prior to the development of the symptoms of

rejections. Applicants further argue that the cited references fails to mentions "acute" or "chronic". The examiner respectfully disagrees.

A claim which unites elements with no change in their respective functions to yield a predictable result is not patentable in the absence of secondary considerations.

For over a half century, the [Supreme] Court has held that a "patent for a combination which only unites old elements with no change in their respective functions ...obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men." Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152 [87 USPQ 303] (1950). This is a principal reason for declining to allow patents for what is obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.

KSR Int'l v. Teleflex Inc., 82 USPQ2d 1385, 1395 (2007).

No explicit teaching is necessary to have led the skilled worker to the particular components – particular timing for administering a therapeutical agent- recited in claims because optimization of result affecting parameters, such as the time of administering a therapeutical agents, would have been within the purview of one or ordinary skill in the art.

The legal conclusion of unpatentability for obviousness depends on four factual inquiries identified by Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966). As applicants acknowledged, These inquiries concern: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) secondary considerations of nonobviousness. Against this background, the obviousness or nonobviousness of the subject matter is determined. KSR Int'l v. TeleflexInc., 127 S. Ct. 1727, 82 USPQ2d 1385, 1388 (2007). In instant case, cyclosporin is known to be an immune suppressive agent and is known to be useful for treating an/or preventing transplant rejection. Further, one or ordinary skill in the art would have understood that the immune activity cause the

transplant rejection. Therefore, if an immunosuppressive agent is expressly taught as be useful for treating transplant rejection, it would have been obvious that the agent be useful for prophylactic treatment of transplant rejections as it treats the underline etiology. Note it is recognized that "A person of ordinary skill is also a person of ordinary creativity, not an automaton." See KSR.

9. Applicants also assert the claims are not obvious as "modification of timing" is note a known option within the technical grasp of a person of ordinary skill in the art, because "neither the trigger not the mechanism of chronic rejections are known," citing Decamp et al for supporting the assertion. The arguments are not persuasive. First, it is not that "for prevention of chronic refractory graft rejection" occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Further, since the references teach broadly the usefulness of cyclosporin for the treatment of transplant rejections without further limitation as to "acute" or "chronic", it would have been obvious to use cyclosporin for treatment of either case. Note since there are only finite number of species (acute, chronic) under the genus of transplant rejection, obvious to try each of the species would have been obvious under 35 U.S.C. 103. see, KSR. Decamp reference merely discusses the detailed mechanism, and does not negate the employment of cyclosporin for treating and/or preventing transplant rejection.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Wang SHENGJUN WANG PRIMARY EXAMINER

Shengjun Wang
Primary Examiner
Art Unit 1617